DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
D1226 B
Food and Drug Administration
7200 Lake Ellenor Drive
Orlando, Florida 32809

CERTIFIED MAIL
RETURN RECEIPT REQUEST

WARNING LETTER

February 27, 1997

FLA-97-27

Steven F. Simmons, President
Nephron Pharmaceuticals Corporation
4131 34th Street
Orlando, Florida 32811

Dear Mr. Simmons:

During the inspection of your firm that covered the period November 4-December 2, 1996, FDA Investigator Brunilda Torres found conditions that are in violation of the Current Good Manufacturing Practice (CGMP) Regulations (Title 21, Code of Federal Regulations, parts 210 and 211). These conditions cause products manufactured by your firm to be considered adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) as follows:

> The validation of critical processes/systems, such as the Steam In Place sterilization process (SIP) and the Clean In Place system (CIP), used in the manufacture of the Sterile Sodium Chloride 0.9% Solution, were not properly performed and completed prior to initiating the distribution of the finished product. Several lots of NaCl solution were distributed prior to completing validation of the sterilization process.
>
> Neither the RO feed water used to generate steam nor the produced pure steam are monitored to assure the bacteriological quality is maintained within acceptable limits.
>
> The environmental monitoring program in place is deficient in that it does not provide for identification of organisms isolated in the controlled areas and does not provide optimum temperatures and incubation time for the isolation of molds and yeasts. Furthermore, a data base of commonly present organisms in the controlled areas has not been established.

At the conclusion of the inspection, a List of Observations including the above mentioned deficiencies and other CGMP related deviations was discussed with you and members of your staff, and a copy left with you.

The above identification of violations is not intended to be all inclusive list at your facility. It is your responsibility to ensure that all drug products are in compliance with the Act, and with CGMP regulations. You should take prompt action to correct these violations. Failure to correct these violations may result in regulatory action, including seizure and/or injunction without further notice. Other Federal agencies are routinely advised of Warning Letters issued so that they may take this information into account when considering the awards of contracts.

We have received your response dated January 2, 1997, to the List of Observations left with you at the close of the inspection, and have the following comments:

> Your response to 5c is inadequate. Incubating your environmental settling plates for 48 hours at 20-25 degrees Centigrade will not give yeasts and molds sufficient time to grow out; optimum is 4-5 days. Subsequently incubating the same plates for 72 hours at 30-35C will allow any bacteria present to further mask the possible presence of any yeasts or molds.

The remainder of your response will be evaluated at our next inspection of your firm. The FDA is prepared to institute an immediate inspection once you provide assurance that the remaining issue discussed above has been satisfactorily addressed, corrections that your response indicated were in process have been completed, and you believe your firm is in complete compliance with CGMP's.

Your further response should be directed to Martin E. Katz Compliance Officer, Food and Drug Administration, 7200 Lake Ellenor Drive, Suite 120, Orlando, Florida 32809, telephone no. (407) 648-6923, ext. 262.

Sincerely,

Douglas D. Tolen

Douglas D. Tolen
Director, Florida District

cc: HFD-324